

Comparison of renal ultrasonography and dimercaptosuccinic acid renal scintigraphy in febrile urinary tract infection

Confronto tra ultrasonografia renale e scintigrafia renale con acido dimercaptosuccinico nelle infezioni urinarie febbrili

Parviz Ayazi¹, Abolfazl Mahyar¹, Elham Noroozian², Neda Esmailzadehha¹, Ameneh Barikani³

¹Metabolic Diseases Research Center, Qazvin University of Medical Sciences, Qazvin, Iran;

²Department of Pediatrics, Qazvin University of Medical Sciences, Qazvin, Iran;

³Children Growth Research Center, Qazvin university of Medical Sciences, Qazvin, Iran

■ INTRODUCTION

Urinary tract infection (UTI) is one of the most prevalent diseases in children, affecting 5% of girls and 0.5% of boys at least once in the lifetime [1-3]. In some researches, the cumulative incidence of UTI in children younger than 6 years has been reported as 3-7% in girls and 1-2% in boys [4]. Pyelonephritis presents with fever, flank pain, and vomiting. In newborns, however, the presenting symptoms are often nonspecific, including restlessness, poor feeding, vomiting, and diarrhea [5]. Pyelonephritis can cause late complications such as hypertension, proteinuria, and even renal failure [6-11].

The accurate diagnosis and early treatment of this disease are essential to prevent or minimize permanent renal damage [8, 12, 13]. Pyelonephritis is diagnosed on the basis of bacteriuria accompanied with clinical symptoms [7, 14]. However, accurate diagnosis of pyelonephritis using only clinical and laboratory results is difficult [13, 15]. Therefore, the diagnostic workup

includes radiological studies, which are a standard of care in primary UTI in children [5, 7, 16]. Renal ultrasonography (US) is a noninvasive, more available and cost-effective method in evaluating some abnormalities of urinary system. It also describes size, shape, position and echogenicity of the kidney and may be helpful in diagnosis of pyelonephritis [17]. Dimercaptosuccinic acid (DMSA) renal scan as another radiologic study is considered to be the most sensitive diagnostic standard for pyelonephritis; however, this method is expensive and involves exposure to radiation [1, 7, 17]. Previous studies have shown the superiority and greater sensitivity of the renal DMSA scan over renal US for the diagnosis of pyelonephritis but Iranian studies are limited [7, 8, 12, 13]. The aim of this study was to assess the sensitivity and specificity of renal US in comparison with renal DMSA scan for the diagnosis of acute pyelonephritis in children with febrile UTI.

■ MATERIALS AND METHODS

This study involved the medical records of children with febrile UTI who had been admitted to the Children's hospital in Qazvin, Iran from Octo-

Corresponding author

Parviz Ayazi

E-mail: parviz_ayazi@yahoo.com

ber 2000 to December 2008. Qazvin is located 150 km northwest of Tehran, the capital city of Iran. The inclusion criteria included patients older than 30 days and younger than five years with signs and symptoms compatible with febrile UTI. In this study, fever with no obvious source, vomiting, reduced desire for food and irritability for infants; abdominal ache and voiding frequency with or without fever for toddlers; and dysuria, frequency, urgency, and abdominal or flank pain with fever for older children were considered as signs and symptoms of UTI [18]. Exclusion criteria were as follows: age >5 years or <30 days; previous history of pyelonephritis or recurrent UTI; absence of ultrasonography/DMSA scan; antibiotic treatment within last 7 days; known concomitant disease and/or any type of renal disorder; previous diagnosis of vesicoureteral reflux; hydronephrosis; renal scars.

UTI was diagnosed on the basis of clinical symptoms, leukocytosis, and positive urine analysis (U/A) and urine culture (U/C). In children younger than two years, urine samples were obtained using catheter. In children older than two years, midstream urine samples were obtained. In children who were not toilet-trained, a catheterized urine sample was obtained to avoid high rate of contamination in a bagged urine sample. The bladder tap was performed after the infant had been well hydrated intravenously or one hour after feeding. Supra-pubic urine was collected by passing a needle through the skin directly into the bladder.

Quantitative urine cultures were performed according to the standard technique. All urine samples obtained by clean void midstream catch, by suprapubic aspiration or by catheterization were sent for culture in less than one hour. All specimens were analyzed at the clinical laboratory of Qazvin Children's hospital.

For the standard U/A, specimen were centrifuged at 2000 RPM for 10 minutes and then examined microscopically for pyuria, reported as the number of leukocyte per high-power field (HPF). Pyuria was defined as at least five White Blood Cell (WBC) per HPF. A loop calibrated to deliver 0.01 mL of urine was used to inoculate plates containing sheep blood agar and MacConkey agar. All plates were inoculated at 35° to 37°C and were examined for colony count and bacterial identification after 24 to 48 hours. UTI was defined as a

single organism $\geq 10^5$ CFU/ml in the U/C or combination of colony count $\geq 10^4$ CFU/ml and symptomatic child if a midstream clean-catch specimen was available [19]. In suprapubic aspirates any organism growth was significant.

The renal US and renal DMSA scan were performed during hospitalization and were interpreted by one expert radiologist. Abnormal renal DMSA scan was the gold standard for diagnosis of pyelonephritis. The criteria for abnormal renal DMSA scan were single or multiple hypoactive areas, centropenia, size discrepancy between both kidneys. In other words, the scintigraphic diagnosis of pyelonephritis was defined by totally or partially reversible lesion on renal DMSA scan. If the first renal DMSA scan examination was abnormal, it was repeated after 6 months. Small or deformed kidneys in renal DMSA scan which might show previous or congenital renal scar were excluded from study. The first renal DMSA scan and renal US was done during the first week of hospitalization. The criteria for abnormal renal US were an increase or a decrease in diffuse or focal parenchymal echogenicity, loss of corticomedullary differentiation, kidney position irregularities, parenchymal reduction, hydronephrosis, hydroureter and increased kidney size [14].

A datasheet was designed to record demographic information, clinical symptoms, laboratory results including WBC count, blood urea nitrogen (BUN), creatinine (Cr), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR); urine (WBC, bacteria, and nitrites), and renal US and renal DMSA scan results. Datasheet was completed based on the information in the patient records. The data collected from the questionnaires were analyzed using a T-test. The significance level was set at $P < 0.05$. The kappa coefficient was used to compare the concordance of the data.

■ RESULTS

One hundred patients met the inclusion criteria, the 79% of them being female. Sixty-three patients were 30 days to 2 years old, and 37 were 2-5 years old. Mean age was 33.26 ± 31.5 months. Demographic and paraclinical findings of the study subjects are shown in Table 1. The most prevalent

Table 1 - Demographics and paraclinical findings in the study subjects.

	Total	Male	female	Age	
				Mean \pm SD	Median
Data analysis	100	21	79	33.26 \pm 31.5	21
Pathological imaging findings	69	17	52	37.6 \pm 33	24
DMSA ^a abnormal	46	10	36	38.8 \pm 32	24
Ultrasonography abnormal	23	7	16	33.6 \pm 32	22
US ^b matched with DMSA (both abnormal)	15	4	11	35.2 \pm 32	24
US matched with DMSA (both normal)	46	8	38	28 \pm 29	18.5
Abnormal DMSA with normal US	31	6	25	40.6 \pm 33	28
Normal DMSA with abnormal US	8	3	5	30.8 \pm 35	14.5
Abnormal WBC ^c	51	9	42	34 \pm 32.1	22
Abnormal UA ^d	76	17	59	32.3 \pm 32.2	19.5
Abnormal U/C ^e	39	8	31	34.6 \pm 32.9	22
Abnormal CRP ^f	50	14	36	42.9 \pm 32.6	40.5
Abnormal ESR ^g	40	10	30	43 \pm 30	40

^aDMSA: Dimercaptosuccinic Acid Renal scintigraphy; ^bUS: Ultrasonography; ^cWBC: white blood cell; ^dUA: Urine Analysis; ^eUC: Urine Culture; ^fCRP: C-reactive protein; ^gESR: Erythrocyte sedimentation rate.

clinical manifestation was fever (74%), followed by signs and symptoms of UTI (42%). U/A was abnormal in 76 patients and 77.65% of them were female. Thirty nine patients had positive U/C and female to male ratio was 31/8. *Escherichia coli* were found to be the pathogenic agent in all positive U/Cs. CRP and ESR were above normal level in 50 and 40 patients, respectively. Renal DMSA scan was abnormal in 46 patients and 36 (88.8%) of them were female. Renal US was abnormal in 23 patients and 16 (70%) of them were female (Tab. 1).

Of the 46 patients who had abnormal renal DMSA scans, only 15 had a concurrent abnormal renal US; thus, comparing results of renal US with renal DMSA scan a significant difference was found between the results ($P \leq 0.03$) and the concordance rate was 18%. Moreover, eight patients with abnormal renal US had normal renal DMSA scan results. Considering the renal DMSA scan as the standard diagnostic test, renal US had a sensitivity of 32%, a specificity of 85%, a positive predictive value (PPV) of 65%, and a negative predictive value (NPV) of 60% for diagnosis of UTI in the present study.

DISCUSSION

Urinary tract infection is very common among children and can cause complications like pro-

teinuria, hypertension, kidney scarring, and chronic kidney disease [1, 7, 17, 20]. The ultimate purpose of treatment is to prevent or reduce the complications of pyelonephritis [7]. Accurate diagnosis of febrile UTI with or without pyelonephritis is difficult using only clinical and laboratory results [12].

Many imaging techniques have been compared for their ability to differentiate UTI with pyelonephritis from UTI without pyelonephritis. US is routinely used to screen renal abnormalities [17]. Voiding cystourethrography (VCUG) is indicated if ultrasonography reveals hydronephrosis, scarring, or other findings that would suggest vesicoureteral reflux (VUR) or obstructive uropathy [21]. Renal DMSA scan is a reliable diagnostic test for pyelonephritis, especially in infants who often have nonspecific clinical symptoms [12]. Although renal US is effective for diagnosis of the urinary tract abnormalities, it is not efficient for diagnosis of renal parenchymal involvement in more than one-third of children with abnormal renal DMSA scan, but normal renal US [12]. In the present study, girls accounted for 79% of the total participants, indicating that the prevalence of UTI with pyelonephritis is higher among girls than among boys.

This finding is consistent with those of most studies on this topic [2, 5, 8, 22]. The most common clinical manifestation was fever, whose incidence was higher than that of urinary signs

and symptoms, indicating that febrile children must be examined for UTI with pyelonephritis. DMSA renal scan was positive for UTI with pyelonephritis in 46% of children, while renal US was positive in only 23% of the affected children. The observed sensitivity, PPV, and NPV are low because the calculation was performed on the total population and not in children with confirmed UTI with pyelonephritis. Therefore, DMSA renal scan, in conjunction with clinical and laboratory data, is more effective for the diagnosis of pyelonephritis than renal US. Consequently, UTI with pyelonephritis will not be detected in a great number of patients if only renal US is used for diagnosis.

Of the 77 patients with normal renal US, 31 (40.2%) had abnormal DMSA renal scans, an inconsistency that warrants greater attention. Of the 46 patients with abnormal DMSA renal scan, 15 had a concurrent abnormal US.

This significant difference shows that when there is access to both tests, DMSA renal scan should be preferred, as it is of greater value than US. Of the 54 patients with normal DMSA renal scan, 8 had abnormal renal US; this difference can be attributed to the following: infections limited to the papilla and medulla may not be detected on DMSA renal scan; the presence of pyelitis alone may result in a normal DMSA renal scan; prematurity of renal tubular function in infants under three months may cause false-negative results of DMSA renal scan; focal perfusion variation resulting from severe vasoconstriction of peripheral arterioles and reduced blood flow; the (focal) diminish in renal perfusion is provoked by edema as inflammatory response of the kidney to bacterial attack, which may result in vascular compression; small kidneys in very young children [7, 13, 5, 23-25].

In the present study, the sensitivity of renal US in diagnosis of UTI without pyelonephritis was rather low (32%); however, its specificity (85%) was acceptable.

Low sensitivity of renal US for the detection of UTI without pyelonephritis has also been reported in other studies [7, 26]. Furthermore, the specificity of renal US observed in the present study are similar to others [1, 13].

The concordance rate of the renal US results with detected UTI without pyelonephritis in the present study was nearly identical to the rates

in other studies [7, 27]. The concordance rate of DMSA renal scan with detected UTI without pyelonephritis in the present study was comparable to those reported previously, and nearly identical to the concordance rate of DMSA renal scan in the group under 1 year of age [28-31]. In the present study, 40.2% patients with abnormal DMSA renal scan had a concurrent normal renal US, which is in agreement with Ataei et al. study (39%) [7].

The concordance of DMSA renal scan and renal US with each other (concurrent abnormal DMSA renal scan and renal US) was highly similar to the results of other studies [22, 30, 32]. Concurrent abnormal renal US and normal DMSA renal scan have been reported in some studies [1, 12]. The results of the present study are in agreement with those of Wang et al. [1].

Hamoui et al. found that 18% of their study patients had abnormal DMSA renal scan; this finding considerably differs from the expected [17]. This difference is possibly because performed DMSA renal scan in patients with normal renal US had a 6-week interval between DMSA renal scan and renal US, which significantly decreases the rate of abnormal DMSA renal scan [17]. The rate of abnormal DMSA renal scans in patients with normal renal US reported by Hamoui et al. is similar to the rate that would have been obtained in the present study if DMSA renal scans had only been performed in patients with normal US. Therefore, the significant difference between the results of the two studies may be attributable to the interval between the DMSA renal scan and renal US in the former study.

The rate of abnormal renal US observed in the present study differs considerably from the rates reported by others [12, 33]. This difference may be due to moderate ischemia, technical factors like interference by intestinal gas, respiratory motion in crying infants, non-cooperation of children, and the expertise of the radiologist [15]. Moreover, false-negative results may have occurred due to partial venous obstruction following edema during the early phase of pyelonephritis, obesity, or even overweight [13, 15]. A summary of the results of relevant studies is shown in Table 2.

US is the best method for diagnosing congenital anomalies and hydronephrosis, which may be accompanied with UTI. It is also suitable for the

Table 2 - Summary of the results of relevant studies.

Reference	N ^a	Abn ^b Sono ^c	Abn DMSA	Abn Sono & Abn DMSA	Nor ^d Sono & Abn DMSA	Abn Sono & Nor DMSA	Sensitivity	Specificity	PPV ^e	NPV ^f
Present study	100	23	46	32.6	40.2	15.3	32	85	65	60
Wang et al. [1]	45	38.9	72.2	-	-	12	49.2	88	91.4	40
Ataei et al. [7]	52	30.7	78.8	-	39	-	40	100	100	30.5
Morin et al. [12]	70	87.1	88.5	93.5	-	37.5	93.5	37.5	-	-
Stogianni et al. [13]	74	-	-	-	-	-	73.8	85.7	67.4	89.1
Dolezel et al. [26]	38	36.8	94.7	-	-	-	41.6	100	-	-

Data are presented as percent. ^aN: number; ^bAbn: Abnormal; ^cSono: Sonography; ^dNor: Normal; ^ePPV: positive predictive value; ^fNPV: negative predictive value.

diagnosis of renal abscess, pyonephrosis, and anomalies of the areas around the kidneys [13]. However, DMSA renal scan is much more valuable than renal US for the diagnosis of UTI with pyelonephritis. DMSA renal scan is not recommended in patients under three months of age owing to the prematurity of the renal cortex and radiation risk [13].

In such patients, renal US (especially power Doppler US) and clinical findings can be used instead of DMSA renal scan.

As the present study was retrospective, data collection and access to the patients were among the limiting factors.

Since absence of US and/or DMSA scan was one of the exclusion criteria in the present study, some children whose renal US and DMSA renal scan results might have affected the results were not examined.

The results of US depend on the operating radiologist's expertise. The long duration of this study and the presence of more than one radiologist were not without effect; however, these conditions better simulate non-experimental and real-life conditions.

In the literature review, the sensitivity of renal US in detection of established renal scarring in children ranged from 37 to 100% [34]. Despite the benefits and accessibility of US, its use in the diagnosis of pyelonephritis is limited. US alone could not be an appropriate test because of low sensitivity for diagnosis of renal parenchymal involvement [22, 35, 36]. Therefore, clinicians should use DMSA renal scan where possible.

However, US should have a more significant role in the imaging algorithm of infants and children with acute UTI, and especially febrile UTI, as it helps to reduce cost and radiation burden in the pediatric population.

Finally this study raises either the question of whether the decision to diagnose UTI without pyelonephritis should be based on the presence of scintigraphic abnormality rather than the result of combination of renal DMSA scan and US, or a second question whether the decision to use antibiotic prophylaxis in children with UTI could be based on the presence of DMSA renal scan and US abnormality rather than only on the presence of low-grade vesicoureteral reflux.

Future research on this topic must involve prospective studies, age-specific results, prolonged follow-up, and comparison of the two tests in order to reduce limitations and obtain comprehensive results. Furthermore, comprehensive results will help identify the optimal imaging protocol for UTI with pyelonephritis, a question as yet unanswered, and will clarify whether non-concordance is present.

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Keywords: urinary tract infection, children, diagnostic imaging, radionuclide imaging, ultrasonography.

SUMMARY

Accurate and early diagnosis and appropriate treatment of patient with urinary tract infection (UTI) are essential for the prevention or restriction of permanent damage to the kidneys in children. The aim of this study was to compare renal ultrasonography (US) and dimercaptosuccinic acid (DMSA) renal scan in the diagnosis of patients with febrile urinary tract infection. This study involved the medical records of children with febrile urinary tract infection who were admitted to the children's hospital in Qazvin, Iran. Pyelonephritis was diagnosed on the basis of clinical symptoms, laboratory tests and abnormal DMSA renal scans. The criteria for abnormality of renal US were an increase

or a decrease in diffuse or focal parenchymal echogenicity, loss of corticomedullary differentiation, kidney position irregularities, parenchymal reduction and increased kidney size. Of the 100 study patients, 23% had an abnormal US and 46% had an abnormal DMSA renal scan. Of the latter patients, 15 had concurrent abnormal US (P value ≤ 0.03 , concordance rate: 18%). Renal US had a sensitivity of 32%, specificity of 85%, positive predictive value of 65% and negative predictive value of 60%. Of the 77 patients with normal US, 31 (40.2%) had an abnormal DMSA renal scan. Despite the benefits and accessibility of renal US, its value in the diagnosis of pyelonephritis is limited.

RIASSUNTO

Una diagnosi accurata e precoce e un trattamento appropriato del paziente affetto da infezione delle vie urinarie (IVU) sono essenziali per prevenire o limitare il danno renale permanente nei bambini. Questo studio è stato condotto nell'intento di confrontare l'ultrasonografia (US) renale e la scansione renale con acido dimercaptosuccinico nella diagnosi di pazienti affetti da IVU febbrile. Lo studio si è basato sulla revisione delle cartelle cliniche di pazienti pediatrici con IVU febbrile ricoverati presso l'ospedale pediatrico di Qazvin, Iran. La diagnosi di pielonefrite è stata posta sulla base dei sintomi clinici, dei test di laboratorio e delle alterazioni delle scansioni renali con DMSA. I criteri utilizzati per definire le alterazioni delle scansioni renali sono stati un aumento o una riduzione dell'ecogenicità

diffusa o focale, la perdita della differenziazione corticomedollare, l'irregolarità della posizione renale, la riduzione parenchimale e l'aumento delle dimensioni renali. Dei 100 pazienti in studio, il 23% presentava una US anormale e il 46% aveva una scansione renale DMSA anormale. Dei 46 pazienti con alterazione della scansione DMSA renale anormale, 15 presentavano una alterazione concomitante della US (P $\leq 0,03$, concordanza 18%). La US renale aveva una sensibilità del 32%, una specificità dell'85%, un valore predittivo positivo del 65% e un valore predittivo negativo del 60%. Dei 77 pazienti con US normale, 31 (40,2%) avevano una scansione renale DMSA alterata. Nonostante i benefici e l'accessibilità correlati alla US renale, il suo valore nella diagnosi di pielonefrite è limitato.

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